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Angela Bardotti

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NOVARTIS VACCINES AND DIAGNOSTICS INC.

INTELLECTUAL PROPERTY- X100B

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EXAMINER

SHAHNAN SHAH, KHATOL S

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.



***Response to Amendment***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/10/2011 has been entered.

***Status of Claims***

2. Claims 1-4, 6-17 and 19-34 are pending. Claims 16, 17, and 19-31 are withdrawn. Claims 1-4, 6-15 and 32-34 are presently under examination. Claims 5 and 18 have been canceled by a previous amendment.

***Rejections Maintained***

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Rejection of claims 1-4, 6-9 and 32-34 under 35 U.S.C. 103(a), made in paragraph 12 of the office action mailed 11/29/2010 is withdrawn in view of applicants' amendments of 3/22/2011.

The rejection was as stated below:

Claims 1-4, 6-9 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bardotti et al. (Vaccine 18: 1982-1993, 3 April 2000) in view of Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54 September 24, 1999). Prior art of record.

The claims are drawn to a method of analyzing a sample's unconjugated saccharide content, comprising the steps of (i) passing the sample through a solid phase extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample.

Bardotti et al. teach a method of analyzing a sample's unconjugated saccharide content, comprising the steps of (i) passing the sample through an extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample ( see abstract, material, methods and table 1). Bardotti et al. teach a glycoconjugate vaccine (see page 1983) single and combined vaccine (see table 1) measuring total sacchride content (see tables 1 and 2). Bardotti et al. teach quantitative conjugate analysis techniques, such as high performance anion exchange chromatography with pulsed amperometric detection (HPAEC-PAD) see abstract. Bardotti et al. do not teach a solid phase extraction device. However, these devices are well known in the art for example Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54, September 24, 1999) teach solid phase extraction, its method development and sorbents (see abstract).

It would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Bardotti et al. to obtain the instant invention. One of ordinary skilled in the art would have been motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of organic solvents in the laboratories which has encouraged the requirement for solvent free procedures and growth of SPE ( see Hennion pages 4-5).

As to limitations of claims 32-34 such as releasing vaccine for use, packaging and adjusting pH. These are considered optimization of experimental parameters. However, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235(CCPA 1955).

5. Applicants' arguments filed 11/10/2011 have been fully considered but they are not persuasive.

Applicants Argue:

- In the Office Action dated June 21, 2011, the examiner states that the Applicants arguments regarding the non-obviousness of Bardotti in view of Hennion presented in the Office Action response filed March 22, 2011 were "fully considered but...not persuasive." (Office Action, page 4). The Examiner then provides various reasons that it would allegedly be obvious for one of skill in the art combine Bardotti and Hennion to arrive at the claimed invention. Applicants respectfully assert that none of these reasons provides an adequate basis for one of skill in the art to combine the references to arrive at the invention of the present claims. As an initial matter, Applicants respectfully assert that the Examiner has improperly assessed the obviousness of the claimed invention by focusing the obviousness analysis on the content of Hennion, rather than on the problems faced by the inventors. In particular, the Examiner's obviousness analysis fails to provide any reason that one of skill in the art interested in methods for the separation of conjugated capsular saccharides from unconjugated capsular saccharides would be motivated to select SPE over many other possible techniques. As described in the present disclosure and as would have been known by one of skill in the art, there are many different methods available in the art that could be tested as an alternative means of separating conjugated capsular saccharides from unconjugated capsular saccharides. One of skill in the art interested in improving the separation of saccharides after reading Bardotti would not immediately and exclusively look to SPE (or any other

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particular technique). Rather, one of skill in the art would consider multiple possible methods for the separation of conjugated capsular saccharides from unconjugated capsular saccharides, in order to attempt to develop an improved method for the separation of saccharides.

- The fact that SPE can be automated does not provide an adequate reason for one of skill in the art to apply SPE to a method for the separation of conjugated capsular saccharides from unconjugated capsular saccharides.
- The fact that SPE provides a large choice of sorbents for trapping analytes over a wide range of polarities also is not an adequate reason for one of skill to apply SPE to the method of Bardotti. Conjugated and unconjugated saccharides are both water-soluble.
- Hennion provides details to determine the main parameters of any sequence (type and amount of sorbent, sample volume which can be applied without loss of recovery, ...) The teachings of Hennion regarding the main parameters of SPE also do not provide an adequate reason for one of skill to apply SPE to the separation of conjugated capsular saccharides from unconjugated capsular saccharides. This content of Hennion is essentially technical information regarding details of various SPE parameters. Technical information regarding SPE does not provide any reason for one of skill in the art who is not using SPE to begin using SPE.
- The fact that materials may be separated by SPE in a few steps, and in some cases, one step, also does not provide an adequate reason for one of skill to apply SPE to the method of Bardotti. One step separation of conjugated capsular saccharides from unconjugated capsular saccharides already existed in the method of Bardotti, in which the saccharides were separated by ultracentrifugation. Accordingly, a person of skill interested in one step separation of saccharides would have no

reason to switch to SPE, since the method of Bardotti already provided one step separation. Moreover, other known techniques available in the art also allowed for the separation of conjugated capsular saccharides from unconjugated capsular saccharides in a single step (e.g. selective precipitation; discussed below). Thus, this teaching of Hennion is also not an "advantage".

- In summary, none of the "advantages" of SPE presented in Hennion provide an adequate reason for one of skill to modify Bardotti in view of Hennion. The cited "advantages" of SPE

presented in Hennion were all either already available in the art for the separation of saccharides (e.g. one-step separation of saccharides; methods may be automated), or they were not relevant to the problem of methods for the separation of saccharides (e.g. SPE provides a large choice of sorbents; Hennion provides technical details regarding SPE methods) at the time of the present invention.

6. In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, it would have been prima facie obvious to one of ordinary skilled in the art at the time of

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invention to use a solid phase extraction device in the method of Bardotti et al. to obtain the instant invention.

It is this office position that Hennion teaches advantages of SPE and being a popular technique in extraction and separation art in and of itself, establish the obviousness of combining that reference with another reference to arrive at a claimed invention” and reduction of organic solvents .

Hennion abstract recites:

“The objective of this review is to provide updated information about the most important features of the new solid-phase extraction (SPE) materials, their interaction mode and then- potential for modem SPE. First, the recent developments are given in formats, phases, *automation*, high throughput purpose and set-up of new types of procedures **Emphasis is then placed on the large choice of sorbents for trapping analytes over a wide range of polarities**, such as highly cross-linked copolymers, functionalized copolymers, graphitized carbons or some specific n-alkylsilicas. The method development is given which is based on prediction from liquid chromatographic retention data or solvation parameters in order can be **to determine the main parameters of any sequence (type and amount of sorbent, sample volume which applied without loss of recovery)**, composition and volume of the clean-up solution, composition and volume of the desorption solution). **Obtaining extracts free from matrix interferences in a few steps one step when possible is now included in the development of SPE procedure.** New selective phases such as mixed-mode and restricted access matrix sorbents or emerging phases such as immunosorbents or molecularly imprinted polymers are reviewed. Selectivity obtained by combining two sorbents is described with the use of ion-exchange or ion-pair sorbents. Special attention is given to **complete automation of the SPE** sequence with its on-line coupling with liquid chromatography followed by various detection modes. This represents a fast, modem and reliable approach to trace analysis.”



7. Rejection of claims 1-4, 6-15 under 35 U.S.C. 103(a), made in paragraph 13 of the office action mailed 11/29/2010 is withdrawn in view of applicants' amendments of 3/22/2011.

The rejection was as stated below:

Claims 1-4, 6-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lei et al. (Dev. Biol (Basel) vol. 103, pp. 259-264, 2000) in view of Hennion, MC. ( Journal of Chromatography A, vol.856, pp. 3-54, September 24, 1999). Prior art of record.

The claims are drawn to a method of analyzing a sample's unconjugated saccharide content, comprising the steps of (i) passing the sample through a solid phase extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample.

Lei et al. teach a method of analyzing a sample's unconjugated saccharide content, comprising the steps of (i) passing the sample through an extraction device to obtain a specimen comprising separated unconjugated saccharide and (ii) analyzing the specimen's saccharide content to give the unconjugated saccharide content of the sample ( see abstract). Lei et al. teach a glycoconjugate vaccine (see abstract) single and combined vaccine, measuring total sacchride content (see abstract). Lei et al. teach limitations of claims 10-15 meningococcal vaccines prepared from *Neisseria meningitis* serogroups A, C, W 135 and Y (see abstract). Lei et al. teach quantitative conjugate analysis techniques, such as high performance anion exchange chromatography with pulsed amperometric detection (HPAEC-PAD) see abstract. Lei et al. do not teach a solid phase extraction device. However, these devices are well known in the art for example Hennion, MC. (Journal of Chromatography A, vol.856, pp. 3-54 September 24, 1999) teach solid phase extraction, its method development and sorbents (see abstract).

It would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Lei et al. to obtain the instant invention. One of ordinary skilled in the art would have been

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motivated by the teachings of Hennion to use a solid phase extraction device (SPE) because of its popularity in sample preparation method and reduction in usage of organic solvents in the laboratories which has encouraged the requirement for solvent free procedures and growth of SPE ( see Hennion pages 4-5).

**8.** Applicants' arguments filed 11/10/2011 have been fully considered but they are not persuasive.

Applicants Argue:

- Turning to the specific reasons to combine raised by the Examiner, the Examiner asserts that in addition to teaching that SPE is a popular technique, Hennion teaches other advantages of SPE that would have provided a reason for one of skill in the art to use SPE in the method of Lei to obtain the claimed invention. The Examiner cites to the same four "other advantages" of SPE disclosed in Hennion, which are discussed at length above regarding Bardotti. Applicants respectfully assert that for the same reasons discussed above regarding Bardotti, none of the "advantages" of SPE presented in Hennion provide an adequate reason for one of skill to modify Lei in view of Hennion .

**9.** In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR*

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*International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, it would have been prima facie obvious to one of ordinary skilled in the art at the time of invention to use a solid phase extraction device in the method of Lei et al. to obtain the instant invention.

It is this office position that Hennion teaches advantages of SPE and being a popular technique in extraction and separation art in and of itself, establish the obviousness of combining that reference with another reference to arrive at a claimed invention” and reduction of organic solvents as mentioned above.

### **Conclusion**

10. No claims are allowed.
11. This is a continuation of applicant's earlier Application No. 10593006. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will

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the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KHATOL SHAHNAN SHAH whose telephone number is (571)272-0863. The examiner can normally be reached on Mon, Wed 12:30-6:30 pm, Thurs-Fri 12:30-4:30pm pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571)-272 0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Khatol S Shahn-Shah/

Examiner, Art Unit 1645

January 16, 2012

/Gary B. Nickol /

**Supervisory Patent Examiner, Art Unit 1645**